

Fat and carbohydrate balances during adaptation to a high-fat diet: letter to the editor

Citation for published version (APA):

Schrauwen, P., van Marken Lichtenbelt, W. D., & Westerterp, K. R. (2000). Fat and carbohydrate balances during adaptation to a high-fat diet: letter to the editor. *American Journal of Clinical Nutrition*, 72(5), 1239-1240. <https://doi.org/10.1093/ajcn/72.5.1239>

Document status and date:

Published: 01/01/2000

DOI:

[10.1093/ajcn/72.5.1239](https://doi.org/10.1093/ajcn/72.5.1239)

Document Version:

Publisher's PDF, also known as Version of record

Document license:

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acids administered might result in a significant rise in plasma amino acid concentrations.

Finally, we agree with Druml that nutritional intervention can alter the course of disease in dialysis patients, with an improvement of morbidity and mortality. However, there are currently no studies designed to investigate the effect of different schedules of amino acid supplementation on the outcome of dialysis patients. Therefore, there is no evidence about the percentage of amino acids that must be retained after supplementation to achieve any beneficial effect. Thus, the value suggested by Druml ($\geq 75\%$) is arbitrary.

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Fat and carbohydrate balances during adaptation to a high-fat diet

Dear Sir:

During consumption of a diet that meets energy requirements, it takes several days before fat oxidation adapts to fat intake when the diet composition is changed from low fat to high fat (1). This finding was confirmed recently by the results of a study by Smith et al (2), who showed a delay in the rise in fat oxidation when the dietary fat content was shifted from 37% to 50% of energy. Smith et al noted that there was a striking degree of variability in the rate of adaptation of fat oxidation to this increased fat intake. According to their data, postabsorptive respiratory quotient, fasting insulin, and maximal oxygen uptake ($\dot{V}O_{2\max}$) were predictors of the capacity to adapt fat oxidation to fat intake.

Although we agree with the conclusion of Smith et al that there is high variability in the capacity to adapt fat oxidation to fat intake, we believe that these data should be interpreted with caution. It is known that there is a clear hierarchy in the maintenance of macronutrient balances, with carbohydrate and protein

balance having the highest priority (3). Fat oxidation, on the other hand, is determined mainly by the difference between energy expenditure and carbohydrate and protein oxidation. Therefore, fat balance is strongly correlated with energy balance. This is where we believe caution should be taken with the interpretation of the data of Smith et al.

In Smith et al's study, the cumulative fat balance over 4 d, when subjects were consuming a high-fat diet in a respiration chamber, was considered to be a good indicator of the capacity to adapt fat oxidation to fat intake. However, because energy balance and fat balance are strongly correlated, the cumulative fat balance over 4 d might just reflect the cumulative energy balance. Although Smith et al proposed to feed the subjects in energy balance, energy balance was not reached on any of the days in the respiration chamber. More important, there was great interindividual variation in the magnitude of energy balance (SEM: 500 kJ/d; $n = 6$). The interindividual variation in fat balance might also reflect the interindividual variation in energy balance. In this respect, it is important to note that in the study by Smith et al, subjects' energy requirements were calculated by multiplying resting metabolic rate by a physical activity index (PAI) factor of 1.5. However, on average, a PAI factor of 1.4 was achieved in the respiration chamber, resulting in positive energy balance. It is known that physical fitness (as could be indicated by $\dot{V}O_{2\max}$) is related to the PAI, ie, the fitter subjects are more active throughout the day (4). This means that subjects with higher $\dot{V}O_{2\max}$ values might have been more active in the respiration chamber (higher PAI) and consequently have showed a less positive energy balance and thus a less positive cumulative fat balance. Thus, the correlation between $\dot{V}O_{2\max}$ and cumulative fat balance might be artificial. The same reasoning might hold for fasting insulin concentrations because physical fitness improves insulin sensitivity (5). It is very likely that, in this situation, energy balance determined the rate of adaptation of fat oxidation to the high fat intake. A situation of zero energy balance should be achieved before conclusions can be made about interindividual variation in the capacity to adapt to high-fat diets.

Second, we believe that the role of glycogen stores cannot be neglected in the interpretation of the data. In his 2-compartment model, Flatt (6) showed that one can adapt fat oxidation to an increased fat intake by 2 mechanisms: 1) expansion of the fat stores or 2) maintenance of the glycogen stores in a lower range. In the short term, and with subjects in (near) energy balance, the first mechanism is of no importance in the adaptation of fat oxidation to fat intake. We showed previously that glycogen stores are indeed important in the rate at which fat oxidation is adapted to a high fat intake (1, 7, 8). Because fat oxidation does not adapt rapidly to the increased fat intake with a high-fat diet, subjects will be in negative carbohydrate balance during the first days of the high-fat diet. This means that they will ultimately lower their glycogen stores, which allows, according to Flatt's model, fat oxidation to increase. Indeed, fat oxidation matched fat intake after several days of consumption of a high-fat diet (1). When glycogen stores were lowered acutely before the start of the experiment, however, both lean and obese subjects were capable of adjusting fat oxidation to a high fat intake within 1 d (7, 8). Because the subjects in the study by Smith et al were in positive energy balance, they probably did not reduce their glycogen stores sufficiently to allow fat oxidation to completely adapt to fat intake. Again, the degree of positive energy balance might have influenced the adaptation.

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Reply to P Schrauwen et al

Dear Sir:

We are pleased that Schrauwen et al considered our article (1) significant enough to comment on the findings. Our study confirmed and, importantly, extended the work of Schrauwen et al (2) on the time course of adaptation to high-fat diets. The overall implication of our work is 2-fold. First, our results show that individuals are highly variable in their ability to switch off carbohydrate oxidation and increase fat oxidation when exposed to a high-fat diet under isoenergetic conditions. Second, we showed that physical fitness and fasting insulin were predictors of an individual's ability to oxidize dietary fat.

The main concern of Schrauwen et al was that our subjects were in positive energy balance and that this confounded our interpretations. This argument assumes that carbohydrate stores drive fat oxidation. Schrauwen et al's previous results (3, 4), based on the use of exercise as a maneuver to deplete

glycogen stores, although confounded, generally support this argument. Contrary to their expectations, energy balance and fat balance in our study were not related. Therefore, the slightly positive energy balance in our study, averaging $\approx 1000 \text{ kJ/d}$ ($\approx 250 \text{ kcal/d}$), cannot account for the observed relations. This observation was noted clearly at the end of the Results section of the article. The subjects in the study by Abbott et al (5), which was cited to support this relation, had energy balances ranging from -3084 to 1958 kJ (-737 to 468 kcal)/d (5). This range of energy balance was clearly greater than what we observed.

Similarly, Schrauwen et al argued that physically fit volunteers [ie, those with a high maximal oxygen uptake ($\dot{V}\text{O}_2 \text{ max}$)] would have higher levels of spontaneous physical activity and therefore more negative energy balances. Again, their assumptions are incorrect. Energy balance was positively related to $\dot{V}\text{O}_2 \text{ max}$ ($r^2 = 0.17$; NS) in the opposite direction to that predicted by Schrauwen et al. This was likely due to our design, which adjusted scheduled physical activity and energy intake on the basis of the previous day's energy balance (detailed in the Methods section).

Regarding the degree to which we were able to maintain energy balance, there are 2 important points to consider. First, in contrast with the protocols of Schrauwen et al, we directly measured both energy intake (duplicate meals) and fecal energy (bomb calorimetry). Accordingly, we avoided the errors inherent when metabolizable energy and dietary intakes are not directly measured. These 2 measured values obviously cannot be obtained during the conduct of the trial. When we used nutrient database values during the conduct of the study, as did Schrauwen et al, our energy balances were also essentially zero.

Last, Schrauwen et al failed to place our results in the context of other existing literature. In rats fed a high-fat diet, skeletal muscle oxidative capacity (6) and insulin sensitivity (7) were predictors of weight gain during high-fat feeding. These results are strikingly similar to our own.

In summary, the concerns of Schrauwen et al are not borne out by our data. Our ability to approach energy balance by using robust measures of energy intake, nonmetabolizable energy output, and indirect calorimetry was one of the major strengths of our investigation. We are confident in our results, which suggest that physical fitness and insulin sensitivity are important predictors of fat balance during acute high-fat feeding.

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